

# CLAIMS

1. An adenosine A<sub>2A</sub> receptor antagonist comprising,  
as the active ingredient, a thiazole derivative  
5 represented by a general formula (I):



(I)

{wherein;

n represents an integer of from 0 to 3;

R<sup>1</sup> represents substituted or unsubstituted cycloalkyl,

- 10 substituted or unsubstituted aryl,  
a substituted or unsubstituted alicyclic heterocyclic  
group, or  
a substituted or unsubstituted aromatic heterocyclic  
group;

- 15 R<sup>2</sup> represents a halogen,  
substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl,  
20 substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic heterocyclic  
group,  
a substituted or unsubstituted aromatic heterocyclic  
25 group,  
substituted or unsubstituted alicyclic heterocyclic-

alkyl,  
substituted or unsubstituted aromatic heterocyclic-  
alkyl,

-NR<sup>5</sup>R<sup>6</sup> (wherein

5 R<sup>5</sup> and R<sup>6</sup> may be the same or different, and each  
represents

a hydrogen atom,  
substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
10 substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted lower alkanoyl,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,

15 a substituted or unsubstituted alicyclic  
heterocyclic group,

a substituted or unsubstituted aromatic  
heterocyclic group,

substituted or unsubstituted alicyclic  
20 heterocyclic-alkyl, or

substituted or unsubstituted aromatic heterocyclic-  
alkyl),

-OR<sup>7</sup> (wherein

R<sup>7</sup> represents a hydrogen atom,

25 substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkanoyl,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,

30 a substituted or unsubstituted alicyclic

heterocyclic group,  
a substituted or unsubstituted aromatic  
heterocyclic group,  
substituted or unsubstituted alicyclic  
5 heterocyclic-alkyl, or  
substituted or unsubstituted aromatic heterocyclic-  
alkyl), or  
-COR<sup>8</sup> [wherein  
R<sup>8</sup> represents a hydrogen atom,  
10 substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
15 substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic  
heterocyclic group,  
a substituted or unsubstituted aromatic  
heterocyclic group,  
20 substituted or unsubstituted alicyclic  
heterocyclic-alkyl,  
substituted or unsubstituted aromatic heterocyclic-  
alkyl,  
-NR<sup>9</sup>R<sup>10</sup> (wherein  
25 R<sup>9</sup> and R<sup>10</sup> may be the same or different, and each  
represent  
a hydrogen atom,  
substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
30 substituted or unsubstituted lower alkynyl,

substituted or unsubstituted lower alkanoyl,  
substituted or unsubstituted lower alkoxy,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
5 substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic  
heterocyclic group,  
a substituted or unsubstituted aromatic  
heterocyclic group,  
10 substituted or unsubstituted alicyclic  
heterocyclic-alkyl, or  
substituted or unsubstituted aromatic  
heterocyclic-alkyl), or  
-OR<sup>11</sup> (wherein  
15 R<sup>11</sup> represents a hydrogen atom,  
substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl,  
20 substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic  
heterocyclic group,  
a substituted or unsubstituted aromatic  
25 heterocyclic group,  
substituted or unsubstituted alicyclic  
heterocyclic-alkyl, or  
substituted or unsubstituted aromatic  
heterocyclic-alkyl)]; and  
30 R<sup>3</sup> and R<sup>4</sup> may be the same or different, and each

represents

a hydrogen atom,

substituted or unsubstituted lower alkyl,

substituted or unsubstituted lower alkenyl,

5 substituted or unsubstituted lower alkynyl,

substituted or unsubstituted aralkyl,

substituted or unsubstituted alicyclic heterocyclic-  
alkyl,

10 substituted or unsubstituted aromatic heterocyclic-  
alkyl,

-COR<sup>12</sup> [wherein

R<sup>12</sup> represents a hydrogen atom,

substituted or unsubstituted lower alkyl,

substituted or unsubstituted lower alkenyl,

15 substituted or unsubstituted lower alkynyl,

substituted or unsubstituted cycloalkyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aralkyl,

20 a substituted or unsubstituted alicyclic  
heterocyclic group,

a substituted or unsubstituted aromatic  
heterocyclic group,

substituted or unsubstituted alicyclic  
heterocyclic-alkyl,

25 substituted or unsubstituted aromatic heterocyclic-  
alkyl,

-NR<sup>13</sup>R<sup>14</sup> (wherein

R<sup>13</sup> and R<sup>14</sup> may be the same or different, and each  
represents

30 a hydrogen atom,

substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted lower alkanoyl,  
5 substituted or unsubstituted lower alkoxy,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic  
10 heterocyclic group,  
a substituted or unsubstituted aromatic  
heterocyclic group,  
substituted or unsubstituted alicyclic  
heterocyclic-alkyl, or  
15 substituted or unsubstituted aromatic  
heterocyclic-alkyl), or  
-OR<sup>15</sup> (wherein  
R<sup>15</sup> represents a hydrogen atom,  
substituted or unsubstituted lower alkyl,  
20 substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,  
25 a substituted or unsubstituted alicyclic  
heterocyclic group,  
a substituted or unsubstituted aromatic  
heterocyclic group,  
substituted or unsubstituted alicyclic  
30 heterocyclic-alkyl, or

substituted or unsubstituted aromatic  
heterocyclic-alkyl)];

provided that,

when R<sup>1</sup> is substituted or unsubstituted phenyl and n is 0,

5 then R<sup>2</sup> is not substituted or unsubstituted 6-oxo-1,6-dihydropyridazin-3-yl},

or a pharmaceutically acceptable salt thereof.

2. The adenosine A<sub>2A</sub> receptor antagonist according  
10 to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

3. The adenosine A<sub>2A</sub> receptor antagonist according  
15 to claim 1 or 2, wherein n is 0.

4. The adenosine A<sub>2A</sub> receptor antagonist according  
to any one of claims 1 to 3, wherein R<sup>2</sup> is substituted or  
unsubstituted lower alkyl, substituted or unsubstituted  
20 aryl, a substituted or unsubstituted alicyclic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group, substituted or unsubstituted alicyclic heterocyclic-alkyl, substituted or unsubstituted aromatic heterocyclic-alkyl, or -COR<sup>8</sup> (wherein R<sup>8</sup> has the  
25 same meaning as defined above).

5. The adenosine A<sub>2A</sub> receptor antagonist according  
to any one of claims 1 to 3, wherein R<sup>2</sup> is substituted or  
unsubstituted aryl.

30

6. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 3, wherein R<sup>2</sup> is a substituted or unsubstituted alicyclic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group.

5

7. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 3, wherein R<sup>2</sup> is -COR<sup>8</sup> (wherein R<sup>8</sup> has the same meaning as defined above).

10

8. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 4 and 7, wherein R<sup>8</sup> is a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, a substituted or unsubstituted alicyclic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group, substituted or unsubstituted alicyclic heterocyclic-alkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl.

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9. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 4 and 7, wherein R<sup>8</sup> is substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted alicyclic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group.

30

10. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 4 and 7, wherein R<sup>8</sup> is



substituted or unsubstituted aryl, a substituted or unsubstituted alicyclic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group.

5           11. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 10, wherein R<sup>3</sup> is a hydrogen atom.

10           12. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 10, wherein R<sup>3</sup> is lower alkyl or aralkyl.

15           13. The adenosine A<sub>2A</sub> receptor antagonist according to claim 11 or 12, wherein R<sup>4</sup> is -COR<sup>12</sup> (wherein R<sup>12</sup> has the same meaning as defined above).

20           14. The adenosine A<sub>2A</sub> receptor antagonist according to claim 11 or 12, wherein R<sup>4</sup> is -COR<sup>12a</sup> (wherein R<sup>12a</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, a substituted or unsubstituted alicyclic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group, substituted or  
25 unsubstituted alicyclic heterocyclic-alkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl).

30           15. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 10, wherein R<sup>3</sup> and R<sup>4</sup> may be the same or different, and each represents -COR<sup>12</sup> (wherein R<sup>12</sup>

has the same meaning as defined above).

16. The adenosine A<sub>2A</sub> receptor antagonist according to claim 1, wherein n is 0; R<sup>1</sup> is a substituted or unsubstituted 5-membered aromatic heterocyclic group containing at least one oxygen atom; and R<sup>2</sup> is -COR<sup>8a</sup> (wherein R<sup>8a</sup> represents a substituted or unsubstituted alicyclic heterocyclic group).

10 17. The adenosine A<sub>2A</sub> receptor antagonist according to claim 16, wherein R<sup>1</sup> is substituted or unsubstituted furyl.

15 18. The adenosine A<sub>2A</sub> receptor antagonist according to claim 16 or 17, wherein R<sup>8a</sup> is a substituted or unsubstituted alicyclic heterocyclic group containing at least one oxygen atom.

20 19. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 10 and 16 to 18, wherein R<sup>3</sup> is a hydrogen atom; and R<sup>4</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl.

25 20. The adenosine A<sub>2A</sub> receptor antagonist according to any one of claims 1 to 10 and 16 to 18, wherein R<sup>3</sup> is a hydrogen atom,; and R<sup>4</sup> is lower alkyl, aralkyl, or aromatic heterocyclic-alkyl.

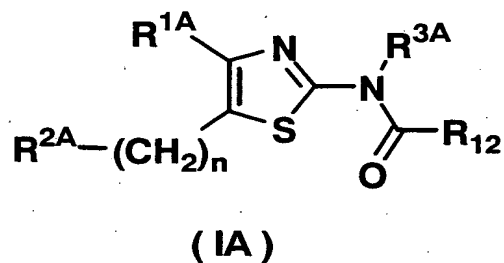
30 21. The adenosine A<sub>2A</sub> receptor antagonist according

to any one of claims 1 to 10 and 16 to 18, wherein R<sup>3</sup> and R<sup>4</sup> may be the same or different, and each represents substituted or unsubstituted lower alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl.

22. An agent for treating and/or preventing diseases associated with adenosine A<sub>2A</sub> receptor comprising, as the active ingredient, a thiazole derivative according to any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof.

23. The agent for treating and/or preventing according to claim 22, wherein the disease associated with adenosine A<sub>2A</sub> receptor is Parkinson's disease.

24. A thiazole derivative represented by a formula (IA):



[wherein R<sup>1A</sup> represents a substituted or unsubstituted 5-membered aromatic heterocyclic group containing at least one oxygen atom (excluding a group selected from 5-phosphonofuran-2-yl and 5-nitrofuran-2-yl); R<sup>12</sup> and n have the same meanings as defined above, respectively;

$R^{3A}$  represents a hydrogen atom;  
substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
5 substituted or unsubstituted aralkyl,  
substituted or unsubstituted alicyclic heterocyclic-  
alkyl,  
substituted or unsubstituted aromatic heterocyclic-  
alkyl, or  
10  $-COR^{12A}$  (wherein  $R^{12A}$  have the same meaning as that of  
 $R^{12}$ ); and  
 $R^{2A}$  represents substituted or unsubstituted lower alkyl,  
substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
15 substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,  
a substituted or unsubstituted alicyclic heterocyclic  
group,  
20 a substituted or unsubstituted aromatic heterocyclic  
group (excluding 2-furyl),  
substituted or unsubstituted alicyclic heterocyclic-  
alkyl,  
substituted or unsubstituted aromatic heterocyclic-  
25 alkyl,  
 $-NR^5R^6$  (wherein  $R^5$  and  $R^6$  have the same meanings as  
defined above, respectively),  
 $-OR^7$  (wherein  $R^7$  has the same meaning as defined above),  
or  
30  $-COR^8$  (wherein  $R^8$  has the same meaning as defined

above)],  
or a pharmaceutically acceptable salt thereof.

25. The thiazole derivative according to claim 24,  
5 wherein  $R^{1A}$  is substituted or unsubstituted furyl, or a  
pharmaceutically acceptable salt thereof.

26. The thiazole derivative according to claim 24  
or 25, wherein n is 0, or a pharmaceutically acceptable  
10 salt thereof.

27. The thiazole derivative according to any one of  
claims 24 to 26, wherein  $R^{2A}$  is substituted or  
unsubstituted lower alkyl, substituted or unsubstituted  
15 aryl, a substituted or unsubstituted alicyclic  
heterocyclic group, a substituted or unsubstituted  
aromatic heterocyclic group, substituted or unsubstituted  
alicyclic heterocyclic-alkyl, substituted or unsubstituted  
aromatic heterocyclic-alkyl, or  $-COR^8$  (wherein  $R^8$  has the  
20 same meaning as defined above), or a pharmaceutically  
acceptable salt thereof.

28. The thiazole derivative according to any one of  
claims 24 to 26, wherein  $R^{2A}$  is substituted or  
25 unsubstituted aryl, or a pharmaceutically acceptable salt  
thereof.

29. The thiazole derivative according to any one of  
claims 24 to 26, wherein  $R^{2A}$  is a substituted or  
30 unsubstituted alicyclic heterocyclic group, or a

substituted or unsubstituted aromatic heterocyclic group,  
or a pharmaceutically acceptable salt thereof.

30. The thiazole derivative according to any one of  
5 claims 24 to 26, wherein  $R^{2A}$  is  $-COR^8$  (wherein  $R^8$  has the  
same meaning as defined above), or a pharmaceutically  
acceptable salt thereof.

31. The thiazole derivative according to claim 30,  
10 wherein  $R^8$  is a hydrogen atom, substituted or  
unsubstituted lower alkyl, substituted or unsubstituted  
lower alkenyl, substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl, substituted or  
unsubstituted aryl, substituted or unsubstituted aralkyl,  
15 a substituted or unsubstituted alicyclic heterocyclic  
group, a substituted or unsubstituted aromatic  
heterocyclic group, substituted or unsubstituted alicyclic  
heterocyclic-alkyl, or substituted or unsubstituted  
aromatic heterocyclic-alkyl, or a pharmaceutically  
20 acceptable salt thereof.

32. The thiazole derivative according to claim 30,  
wherein  $R^8$  is substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl, a substituted or  
25 unsubstituted alicyclic heterocyclic group, or a  
substituted or unsubstituted aromatic heterocyclic group,  
or a pharmaceutically acceptable salt thereof.

33. The thiazole derivative according to claim 30,  
30 wherein  $R^8$  is substituted or unsubstituted aryl, a

substituted or unsubstituted alicyclic heterocyclic group, or a substituted or unsubstituted aromatic heterocyclic group, or a pharmaceutically acceptable salt thereof.

5        34. The thiazole derivative according to any one of claims 24 to 33, wherein  $R^{3A}$  is a hydrogen atom, or a pharmaceutically acceptable salt thereof.

10       35. The thiazole derivative according to any one of claims 24 to 33, wherein  $R^{3A}$  is lower alkyl or aralkyl, or a pharmaceutically acceptable salt thereof.

15       36. The thiazole derivative according to any one of claims 24 to 33, wherein  $R^{3A}$  is  $-COR^{12A}$  (wherein  $R^{12A}$  has the same meaning as defined above), or a pharmaceutically acceptable salt thereof.

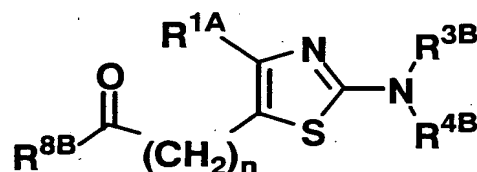
20       37. The thiazole derivative according to claim 36, wherein  $R^{12A}$  is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, a substituted or unsubstituted alicyclic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group, 25 substituted or unsubstituted alicyclic heterocyclic-alkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl, or a pharmaceutically acceptable salt thereof.

30       38. The thiazole derivative according to any one of claims 24 to 37, wherein  $R^{12}$  is substituted or

unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, a substituted or unsubstituted alicyclic heterocyclic group, a substituted or unsubstituted aromatic heterocyclic group, substituted or unsubstituted alicyclic heterocyclic-alkyl, or substituted or unsubstituted aromatic heterocyclic-alkyl, or a pharmaceutically acceptable salt thereof.

10

39. A thiazole derivatives represented by a formula (IB):



(IB)

(wherein

15 n and R<sup>1A</sup> have the same meanings as defined above, respectively;

R<sup>3B</sup> represents a hydrogen atom,

substituted or unsubstituted lower alkyl,

substituted or unsubstituted lower alkenyl,

20 substituted or unsubstituted lower alkynyl,

substituted or unsubstituted aralkyl,

substituted or unsubstituted alicyclic heterocyclic-alkyl, or

substituted or unsubstituted aromatic heterocyclic-alkyl;

25

R<sup>4B</sup> represents substituted or unsubstituted lower alkyl,



substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted aralkyl,  
substituted or unsubstituted alicyclic heterocyclic-  
5 alkyl, or  
substituted or unsubstituted aromatic heterocyclic-  
alkyl; and

R<sup>8B</sup> represents a hydrogen atom,

substituted or unsubstituted lower alkyl,  
10 substituted or unsubstituted lower alkenyl,  
substituted or unsubstituted lower alkynyl,  
substituted or unsubstituted cycloalkyl,  
substituted or unsubstituted aryl,  
substituted or unsubstituted aralkyl,

15 a substituted or unsubstituted alicyclic heterocyclic  
group,

a substituted or unsubstituted aromatic heterocyclic  
group,

substituted or unsubstituted alicyclic heterocyclic-  
20 alkyl, or

substituted or unsubstituted aromatic heterocyclic-  
alkyl),

or a pharmaceutically acceptable salt thereof.

25 40. The thiazole derivative according to claim 39,  
wherein R<sup>1A</sup> is substituted or unsubstituted furyl, or a  
pharmaceutically acceptable salt thereof.

41. The thiazole derivative according to claim 39  
30 or 40, wherein n is 0, or a pharmaceutically acceptable

salt thereof.

42. The thiazole derivative according to any one of claims 39 to 41, wherein  $R^{8B}$  is a substituted or unsubstituted alicyclic heterocyclic group containing at least one oxygen atom, or a pharmaceutically acceptable salt thereof.

43. The thiazole derivative according to any one of claims 39 to 42, wherein  $R^{3B}$  is a hydrogen atom, or a pharmaceutically acceptable salt thereof.

44. The thiazole derivative according to claim 43, wherein  $R^{4B}$  is lower alkyl, aralkyl or aromatic heterocyclic-aralkyl, or a pharmaceutically acceptable salt thereof.

45. A pharmaceutical composition comprising, as the active ingredient, a thiazole derivative according to any one of claims 24 to 44, or a pharmaceutically acceptable salt thereof.

46. An adenosine  $A_{2A}$  receptor antagonist comprising, as the active ingredient, a thiazole derivative according to any one of claims 24 to 44, or a pharmaceutically acceptable salt thereof.

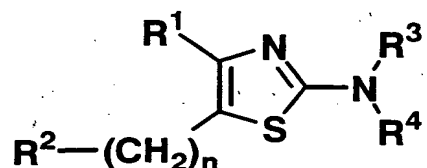
47. An agent for treating and/or preventing diseases associated with adenosine  $A_{2A}$  receptor comprising, as the active ingredient, a thiazole derivative according

to any one of claims 24 to 44, or a pharmaceutically acceptable salt thereof.

48. An agent for treating and/or preventing central nervous system diseases comprising, as the active ingredient, a thiazole derivative according to any one of claims 24 to 44, or a pharmaceutically acceptable salt thereof.

49. An agent for treating and/or preventing Parkinson's disease comprising, as the active ingredient, a thiazole derivative according to any one of claims 24 to 44, or a pharmaceutically acceptable salt thereof.

50. A method for treating and/or preventing diseases associated with adenosine A<sub>2A</sub> receptor, which comprises administering an effective amount of a thiazole derivative represented by a general formula (I):



(I)

(wherein n, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> have the same meanings as defined above, respectively), or a pharmaceutically acceptable salt thereof.